Electrolyte Abnormalities in Neonates

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Electrolyte abnormalities Critically ill neonates

- Frequently occur
- Usually mild disturbances
  can be life-threatening
- Epiphenomena
  Reflecting organ dysfunction
    - Gastrointestinal
    - Renal
    - Endocrine

  Reflecting global insult
- Iatrogenic
  Fluid therapy errors
  Feeding mishaps
- Fetal to neonatal physiology transition

Electrolyte Abnormalities

- Sodium/Water Balance
- Hyponatremia/Hypernatremia
- Hypokalemia/Hyperkalemia
- Hypocalcemia/Hypercalcemia
- Hypomagnesemia/Hypermagnesemia

Sodium/Water Balance

- Transition from fetal physiology
  - Late term fetus
    - High F_{xNa}
  - Transition – to low F_{xNa}
    - Most species during 1st day
    - Fetal foal - before birth
- Sodium conserving mode
  - Na requirement for growth
    - Bone growth
    - ↑ body mass
      - Increase in interstitial space
  - Milk diet
    - Fresh milk is sodium poor
      - 9-15 mEq/l

Sodium/Water Balance
Sodium Conservation

- Neonatal kidney less able to excrete Na load rapidly
- ↓ GFR
- Glomerulotubular balance
  - Absorption Na in proximal tubule balanced with snGFR
  - Adult – distal tubule modulated based on Na balance
  - Neonate – both proximal and distal tubules
  - Distal important compensatory mechanism
    - Retention Na for growth
    - No autoregulation GFR at neonatal BP
    - Disruption Na reabsorption capacity proximal tubules
      - Hormones – cortisol, ANP
      - Hypoxia
      - Increased arterial pressure
- Compensatory mechanism
  - Compensate for uncertain proximal tubule function
  - Does not change with Na intake
  - Limits neonates ability to excrete Na loads rapidly

Sodium/Water Balance
Sodium Overload

- Sodium containing intravenous fluids
  - 6-7.25 mEq Na/kg/day
  - Mare's milk – 1.8 mEq Na/kg/day
  - 3-4 X normal Na
- Sodium overloading
  - Expansion of the extracellular fluid space
  - Sodium fractional excretion will remain low
- Difficulty dealing with volume loading

Sodium/Water Balance
Sodium Overload

- Confounding influences
  - Glucose diuresis
  - Fluid diuresis
    - Na containing fluid boluses
  - Diuretic induced diuresis
  - Renal tubular disease
    - Hypoxia
- Inability to rapidly excrete a volume load
  - Fluid shifts – intravascular:interstitial space
  - Neonate's inability excrete excess volume
  - Neonates Na conservation

Hyponatremia

Hyponatremia

Spurious hyponatremia

Dilutional hyponatremia

Depletional hyponatremia

Redistribution hyponatremia

Hyponatremia

- Na stores determines ECF volume
- Na concentration (osmolality) – water balance
- Tonicity
  - Hypotonic hyponatremia
    - Water excess relative to Na stores
    - Na stores
      - Decreased
      - Normal
      - Increased
  - Isotonic hyponatremia
  - Hypertonic hyponatremia

Spurious Hyponatremia

- Normal plasma sodium concentration
- Laboratory reports a low concentration

Presence of interfering substances

- Lipids
- Artificially dilutes sample

Mistakes in sampling

- Venipuncture site distal to a ↓Na drip
- Sample is taken from a catheter

  Infusion of a ↓Na solution

  Insufficient dead space clearing

Dilutional Hyponatremia

- Lack of balance – fluid intake/urine output
- Loss of integrity of the urinary system
  - Ruptured bladder
  - Ruptured/necrotic urachus
  - Fenestrated ureters
- Renal failure
- Failed/delayed renal transition
  - Fetal to neonatal physiology
- Water overload
  - Management mistakes
    - Dilute milk replacer
    - Excessive water enemas (retained)
    - Fluid therapy errors (Na wasting renal syndromes)
  - Syndrome of inappropriate antidiuresis (SIA)

Dilutional Hyponatremia

- Most common form hyponatremia in neonates
- Only occurs with intake of hyponatremic fluid
  - Fresh milk
  - Hyponatremic rehydration formulas
    - Dextrose in water or half strength saline
- Not with isotonic Na containing fluids
  - Normisol-R, Lactated Ringers, Plasmalyte
  - Less marked on milk replacer than fresh milk

Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- Synonym: SIADH
  - Syndrome of Inappropriate Antidiuretic Hormone Secretion
- Hyponatremia secondary to
  - Inappropriate reabsorption of water from urine
- Diagnosis
  - High urine osmolarity
  - Hyposmolar hyponatremia - plasma
  - Normal renal function
  - Normal adrenal function
  - Euvolemia
- Can have excessive renal sodium excretion
  - Often absent in the neonate
  - Low sodium intake

Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- Clinical syndrome
  - Sudden decrease in urine output
  - High urine specific gravity
  - Weight gain
    - 10-15% of body weight overnight
  - No edema
  - Decreasing plasma sodium concentration

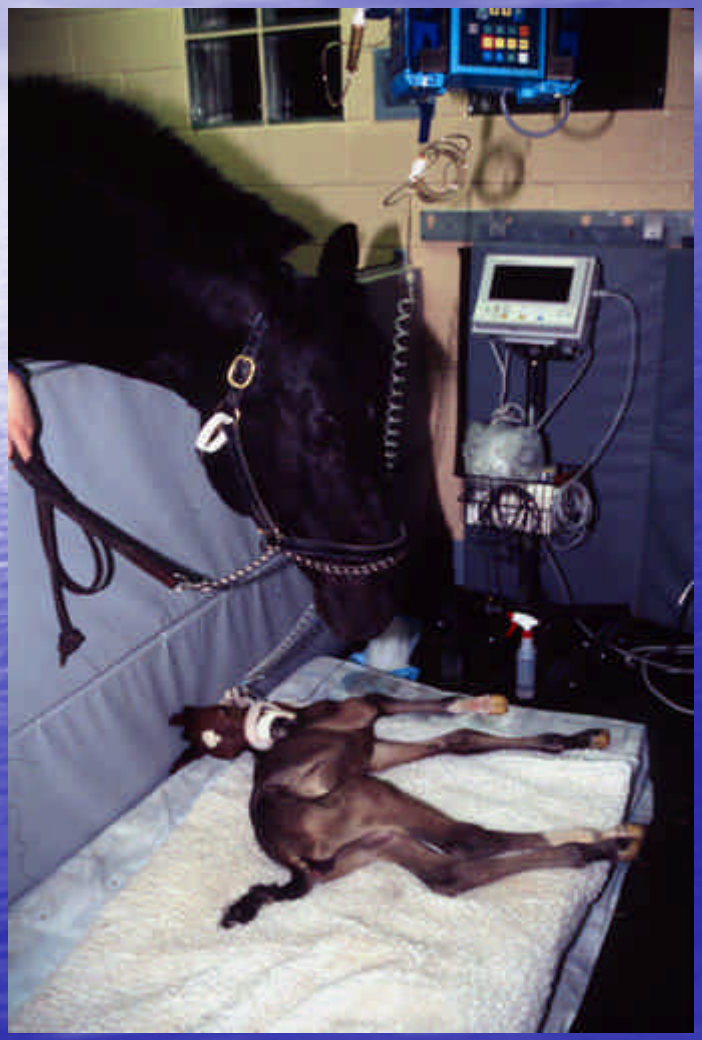
Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- SIADH
  - Inappropriate vasopressin release
    - Erratic and unpredictable release vasopressin
    - Reset of the osmostat
      - Threshold for release is lowered
    - Vasopressin release not fully suppressed at low osmolarity
      - But normal at higher osmolarity
  - Receptor abnormality (vasopressin release normal)
    - Hypersensitive receptors
    - Receptors continue to respond
      - After vasopressin levels decrease
      - Hypovasopressinemic antidiuresis

Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- SIAD not SIADH
  - High urine osmolarity
  - Hyposmolar hyponatremia
  - Hypovolemia
    - Appropriate vasopressin release
    - Defense of volemia
- Diuretics
- Abnormal adrenal function
- Abnormal renal function

Depletional Hyponatremia



- Na loss > water
- Diarrhea
  - Excessive sodium loss in feces
  - Rehydration with Na poor fluids
    - Fresh/frozen milk
    - Fresh water
- Renal sodium wasting
  - Tubular disease
  - Use of diuretics
  - Endocrine disturbances
  - Rehydration with Na poor fluids
    - Fresh/frozen milk
    - Fresh water

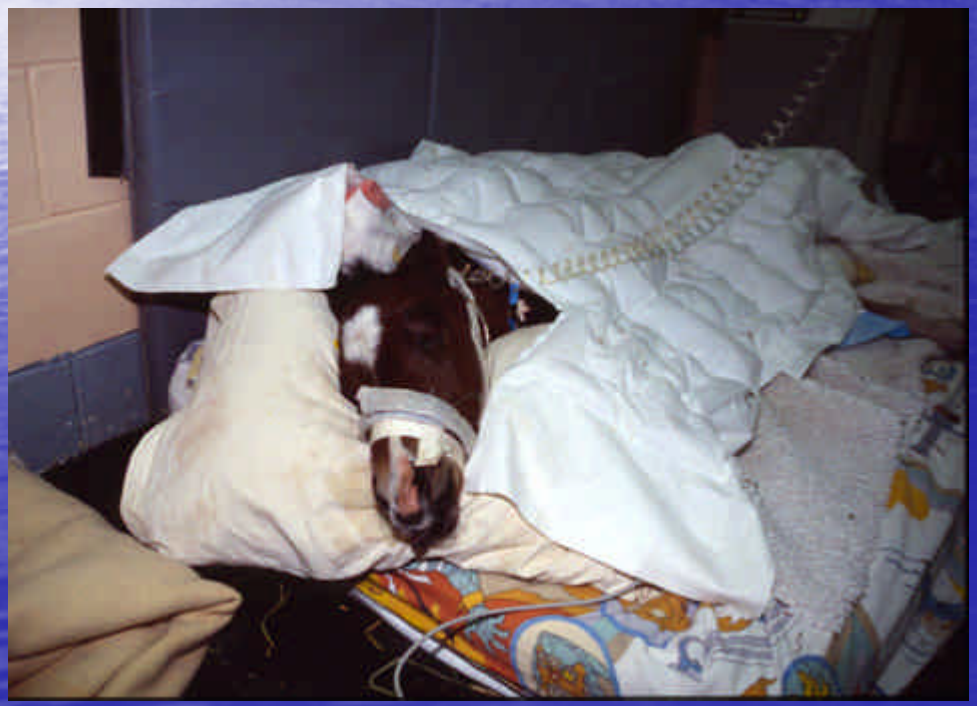
Redistribution Hyponatremia

- Low sodium concentration
  - Osmolarity normal
  - Isosmotic hyponatremia
    - Hyperosmotic hyponatremia
- Other osmotically active particles present
  - Redistribute fluid from intracellular space
    - Appropriate decrease Na concentration
    - Hyperglycemia

      $Na_{corrected} = Na_{measured} + [(Glu - 90)/36]$
    - Iatrogenic addition of osmoles

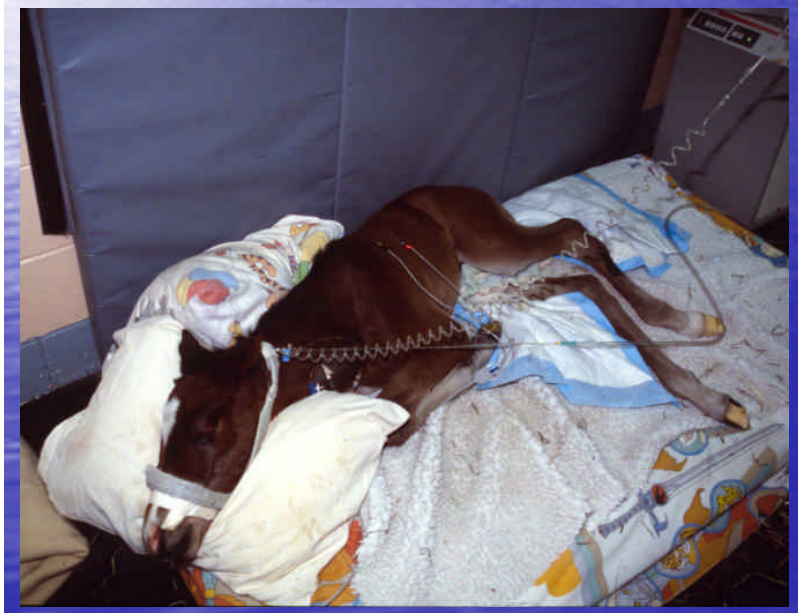
      Mannitol
    - Secondary to sick cell syndrome

Hyponatremia
Sick Cell Syndrome



- Critically ill patients
  - Cellular insult
  - Loss of cell wall integrity
  - Solutes leak
    - Fluid follows
    - Dilution of extracellular sodium levels

Hyponatremia
Sick Cell Syndrome



- Redistribution hyponatremia

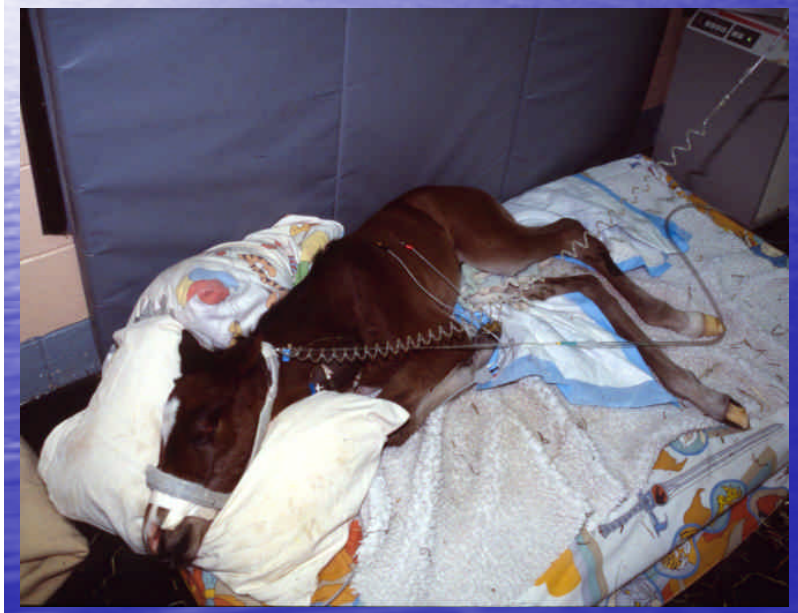
  "Osmolar Gap"

  - Osm_{calc}= 2XNa (mEq/l) + urea (mg/dl)/2.8 + glucose (mg/dl)/18
  - $Osm_{Gap} = Osm_{measured} - Osm_{calc}$
  - Unmeasured osmolites

  Osm_{Gap} > 10 mOsm

  - multiorgan dysfunction (MODS)
  - ↑ fatality rate in ICU patients

Hyponatremia
Sick Cell Syndrome



- Which solutes??

  Traditional
  - Organic phosphates
  - Pyruvate
  - Lactate
  - Amino acids

  Recent studies
  - Failed to identify major components

Hypotonic Hyponatremia Treatment

- Recognize cause
  - Don’t treat spurious, redistribution hyponatremia
- Symptomatic – euvolemia/hypervolemia, with concentrated urine
  - Hypertonic saline
  - Furosemide – limit volume expansion
  - Stop water intake
- Symptomatic – hypovolemia
  - Isotonic saline
- Mild symptomatic – dilute urine
  - Evaporative losses only

Hypotonic Hyponatremia Treatment

- Treat until signs subside
  - Increase serum Na 3-7 mmol/l
- Avoid osmotic demyelination
  - Don't increase Na faster than 8-10 mmol/day
    - Can increase 1 mmol/hr 1st few hrs then slow
- Asymptomatic – slow rise
  - Begin with half strength fluids after urinary tact repair to slow rise
  - Often difficult to control rate of rise
  - Faster onset (hours) – faster correction tolerated
  - Some question risk of osmotic demyelination
  - Water restriction may be all that is needed

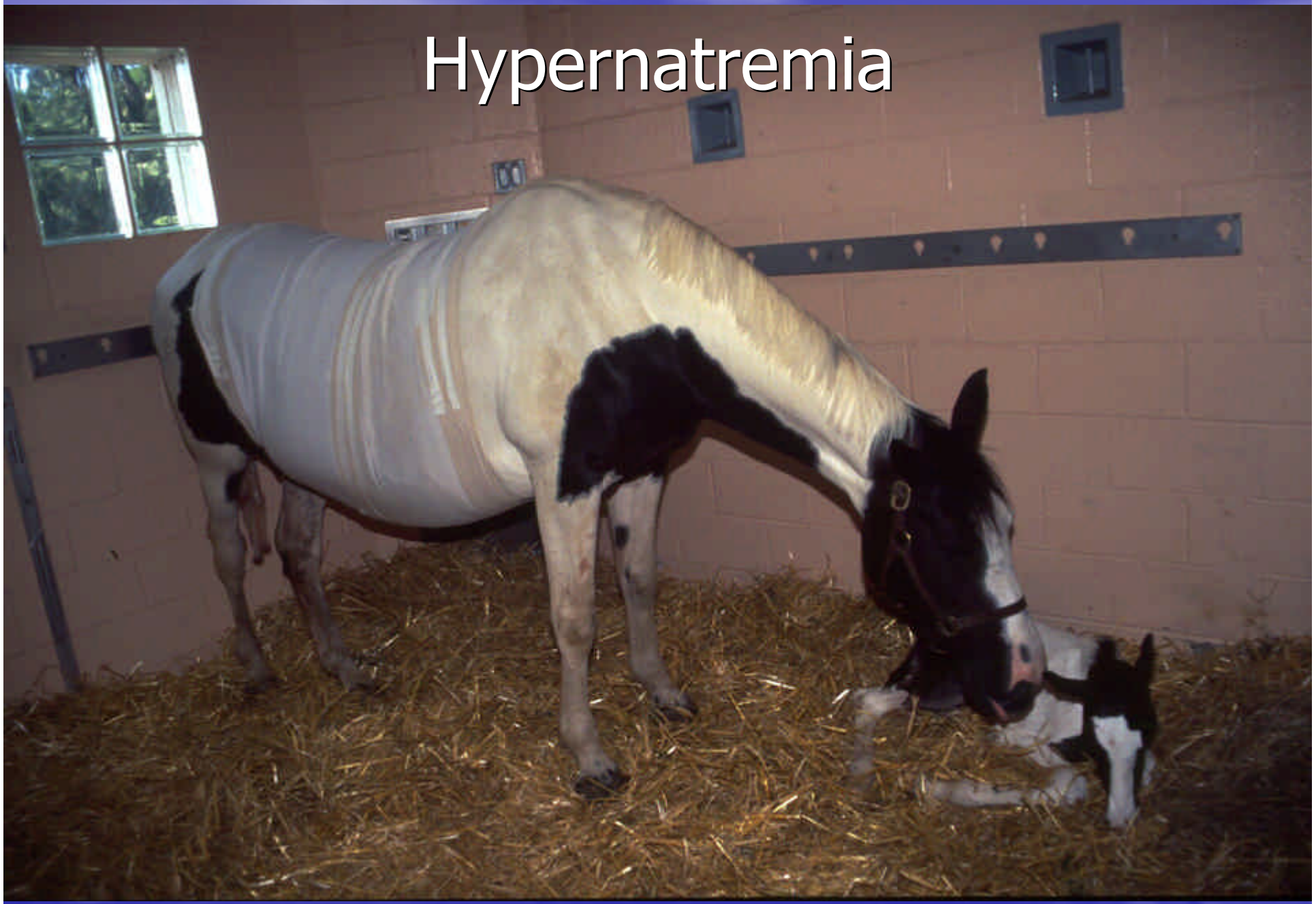
Hypotonic Hyponatremia
Estimate Effect of Infusate

$$\text{For each liter given Change in serum [Na]} = \frac{(\text{Infusate Na} + \text{Infusate K}) - \text{serum Na}}{\text{Total body water} + 1}$$

Total body water

- early neonate = 0.75 X body wt
- pediatric = 0.6 X body wt
- adult = 0.5-0.6 X body wt
- geriatric = 0.45-0.5 X body wt

Hypernatremia



Hypernatremia

- Uncommon
- Deficit of water relative to Na stores
- Hypertonic hyperosmolality
- Causes of hypernatremia
  - Spurious
  - Excessive free water loss
    - Pure water loss
    - Hypotonic fluid loss
  - Hyperosmotic intake
  - Iatrogenic

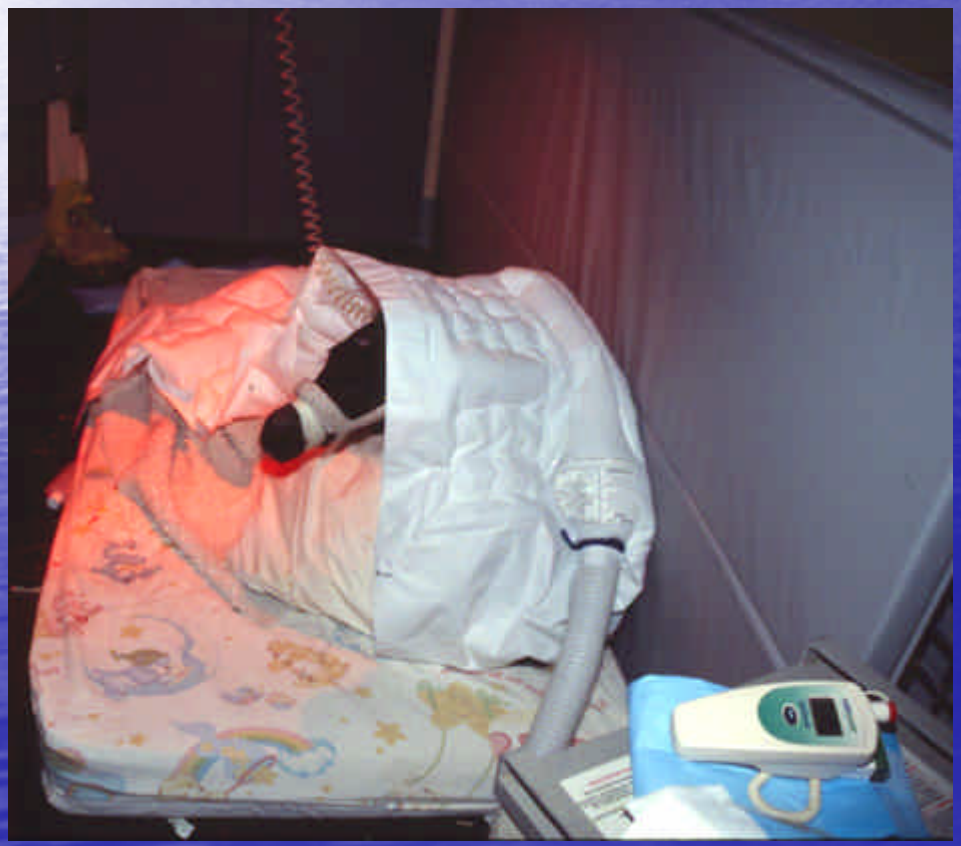
Spurious hypernatremia

- Sampling errors

  Blood samples from the intravenous catheter

  - Not large enough presample
  - Sample contamination with saline

Hypernatremia
Increased free water loss



Increased insensible loss

- Increased respiratory rate
- Low humidity
- High body temperature
- External warming
  - Radiant heat
  - Hot air heat

Increased insensible loss with limited intake

- Hot weather
- Neonate unable to nurse
  - Lack opportunity
  - HIE

Hypernatremia
Increased free water loss

- Water loss
  - Diabetes insipidus
    - Unusual because of neonate's diet
- Hypotonic fluid loss
  - Furosemide
  - Osmotic diuresis
    - Glucosuria
    - Mannitol
  - Renal disease
  - Diarrhea
  - Excessive sweating

Hypernatremia
Hyperosmotic Intake

- High sodium maternal milk
  - Excessive sodium intake relative to free water
- Iatrogenic mishaps
  - Improperly mixed electrolyte solutions
    - Without the opportunity/ability to drink fresh water
  - Improperly mixed milk replacers
    - All powdered milk replacers are sodium rich
  - Use of hypernatremic intravenous fluids solutions
    - 5% sodium bicarbonate
    - Hypertonic saline
  - Use of saline in oxygen humidifiers
  - Hypertonic enemas (retained)

Hypernatremia Treatment

- Recognize cause
  - Eliminate/manage underlying problem
- If developed acutely (hours)
  - Can be corrected over hours (↓Na 1 mmol/hr)
  - Usually acute sodium loading
- If developed slowly (over days)
  - Intracellular accumulation organic osmolytes
  - Correct slowly to avoid cerebral cellular edema
  - ↓Na < 0.5 mmol/hr (target ↓Na 10 mmol/day)
- Oral fluid therapy
  - Na and K in milk

Hypernatremia
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Total body water

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Hypokalemia

Hypokalemia

- Hypokalemia common in neonates
- Anabolic increase in cell mass (growth)
  - Potassium major intracellular ion
- Renal K wasting
  - Diuresis
  - Renal pathology

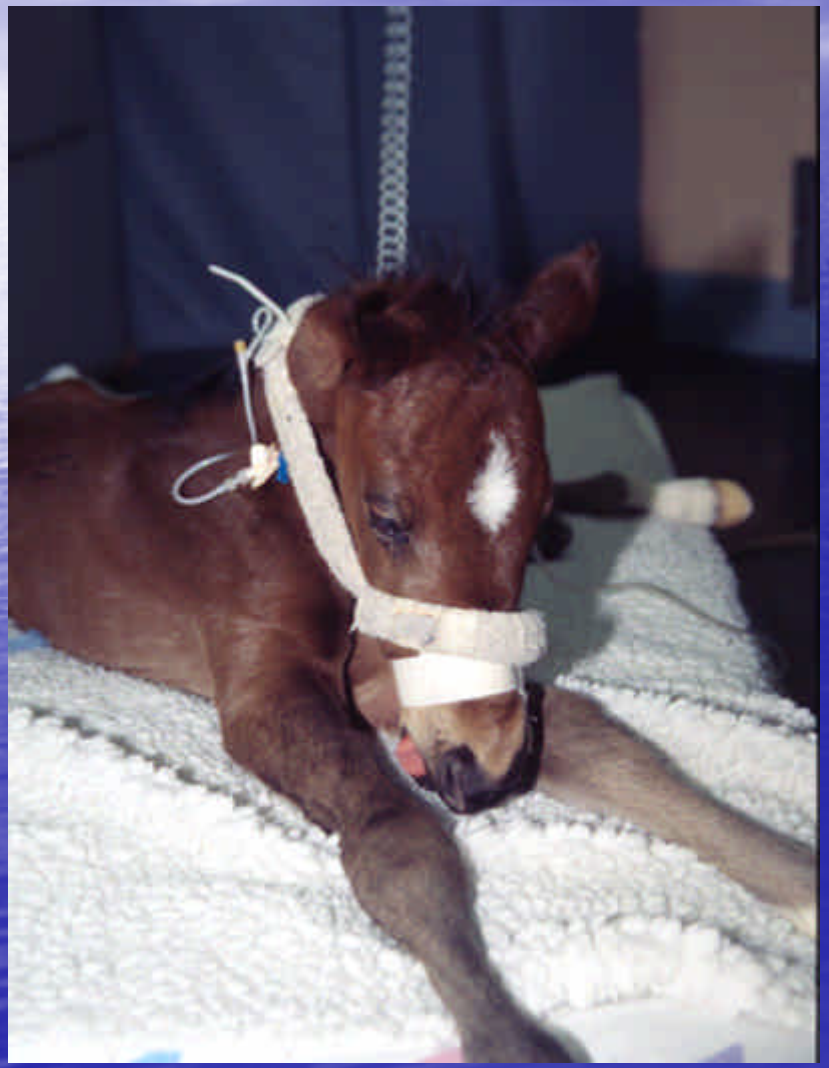
Hypokalemia

- Stress/sepsis hypokalemia
  - Resting muscle
    - uses 10% of available Na^+:K^+ ATPase activity
  - Stimulated acutely by
    - Insulin
    - Epinephrine
    - ↑ intracellular Na
    - Contractile activity
  - Stress/Sepsis →↑ epinephrine
    - ↑ Na^+:K^+ ATPase activity
    - Significant intracellular shifts of K → hypokalemia
    - ↑ ATPase demand
      - ↑ glucose utilization/requirement
      - ↑ glucose transport into the cell resulting → further shift K intracellular

Hypokalemia

- High levels of potassium in milk
  - will support growth requirements
- Stressed/Septic neonates
  - Not tolerate oral feeding
- Neonates require significant K supplementation
  - Prolonged intravenous glucose
  - Parenteral nutrition
  - Limited or no milk feeding
- Glucocorticoid administration
  - Mineralocoritcoid receptor stimulation
  - → urine loss of potassium

Hyperkalemia



- Differetial diagnosis
  - Ruptured bladder
  - Urinary tract defect
  - Sick cell syndrome
  - Iatrogenic
  - Protein catabolism

Hyperkalemia

- Loss of integrity lower urinary tract
  - ↑K only when on a milk diet
    - Also true for ↓Na, ↓Cl
  - Receiving parenteral nutrition
    - ↑K only occur with overzealous parenteral K administration
- Sick cell syndrome
  - Suffer global cell insult
    - Perinatal hypoxic ischemic asphyxial insults
  - ↑K = 6-8 mEq/l
- Iatrogenic in the face of renal insufficiency
- Protein catabolism - mild hyperkalemia

Hypocalcemia

- ↓ plasma Ca^{++}
  - Fetal to neonatal physiology transition
  - Active placental transport high levels of Ca
  - At birth
    - Neonate's homeostatic mechanisms begin regulation
- Parathyroid hormone (PTH)
  - Level is low at birth
    - Slow to respond
  - PTH requires
    - Mg & Vitamin D
      - Both initially deficient

Hypocalcemia

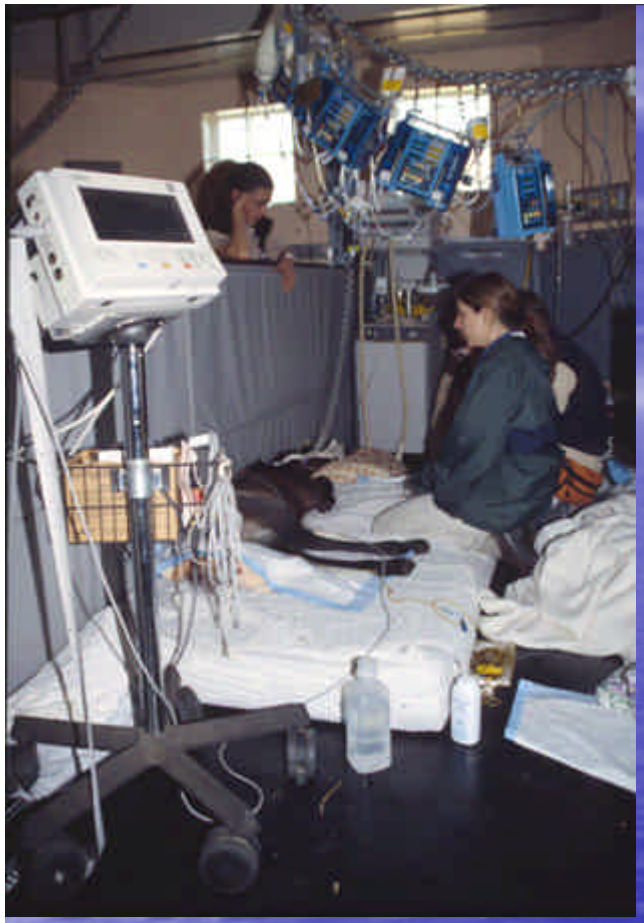
- Calcitonin
  - At birth high levels
  - Further increase calcitonin
    - Hypoxic ischemic asphyxia
    - Prematurity
- Ca^{++} levels
  - Decrease during the first hours after birth
  - Will stabilize and slowly rise
    - If no confounding factors

Hypocalcemia

- Neonatal alkalosis
  - Intrauterine catabolism
  - Catabolism during neonatal period
  - → persistently low calcium levels
- Neonate well adapted to low Ca^{++}
  - Treatment not indicated
- Extremely low Ca^{++} levels at birth
  - Suggest significant intrauterine distress

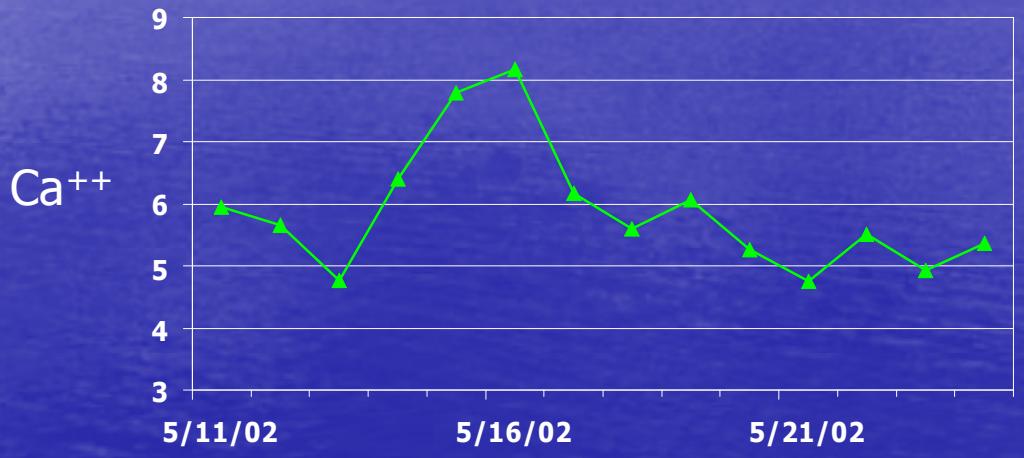
Hypercalcemia

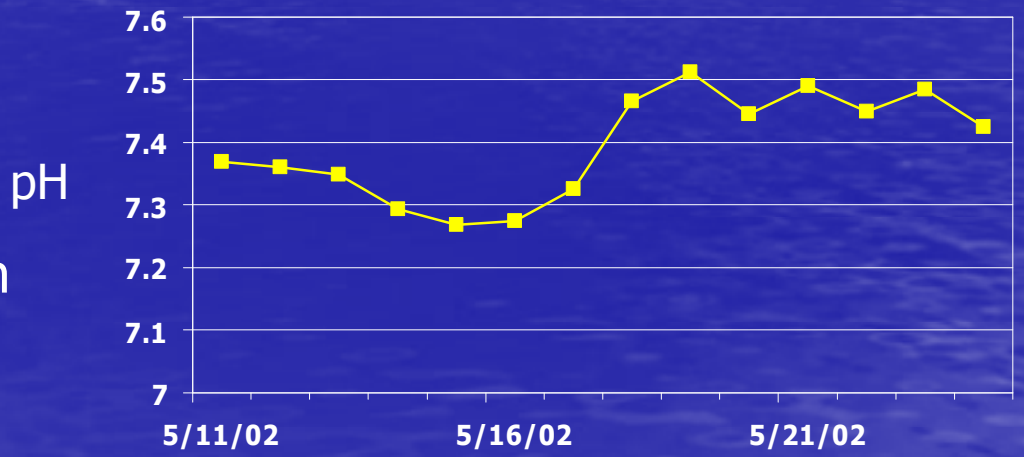
- Ca^{++} high at birth
  - 6-7 mg/dl
  - Active placental transport
- High levels transient
  - Decreasing within hours
  - Unless significant metabolic acidosis
- Unusually high ionized at birth
  - Ca^{++} = 10-20 mg/dl
  - Suffered significant intrauterine distress
- In response to acidosis
  - Theoretical cause but not usually seen



Hypercalcemia and Acidosis

Premature
Incomplete Ossification
Sepsis
Neonatal encephalopathy
Neonatal metabolic maladaptation
Neonatal gastroenteropathy
Neonatal nephropathy





Hypomagnesemia

- Mg actively transported across the placenta
  - Transport adversely affected by
    - Placental insufficiency
    - Low maternal blood levels
  - May be born with hypomagnesemia
- ↓Mg at birth
  - Reflect total body deficiency
    - ~50% of total body Mg - soft tissues and plasma
  - ↓Mg not abnormal homeostasis
    - as is true with calcium

Hypomagnesemia

- ↓Mg can be accompanied by ↓Ca
  If persistently ↓Ca
  - Investigate ↓Mg
  - PTH requires normal Mg
  - Treating with Ca may exacerbate the problem
  - Ca will compete with Mg for transport
  - Treatment with Mg may readily remedy hypocalcemia
- ↓Mg will also occur associated with
  High phosphate levels
  Diarrhea
  Excessive renal loss
- ↓↓↓K
  Require Mg therapy before K will increase

Hypermagnesemia

- Unusual in the neonate
- Iatrogenic errors
  - $MgSO_4$ infusions
    - Treating hypoxic ischemic encephalopathy
    - Overzealous treatment
- Signs
  - Mild central depression
  - Not associated with hypotension

Cases

- Hypernatremia
- Hyperkalemia

  Two Mur

  Yankee
- Redistribution Hyponatremia

  Hugsie
- SIAD

Vinnie

- History
  - Day 353 gestation.
  - Could not stand – weak
- Referred - 15 hr old
  - Post maturity
  - Neonatal encephalopathy
    - Hyperresponsiveness
    - Poor balance
- Early sepsis

Vinnie
Hospital Course

- Day 2

  Improve strength, ability to stand

  Was learning to nurse the mare

  Periods of central tachypnea

    - Occasional ataxic breathing

  Urinated infrequently

Vinnie
Hospital Course

- Day 3

  Neurologic signs

  - Tachypnea with breath-holding episodes
  - Held his tongue out to the right side of mouth
  - Continued hyperresponsive, poor balance

    Runs into things

    Circling - large circles

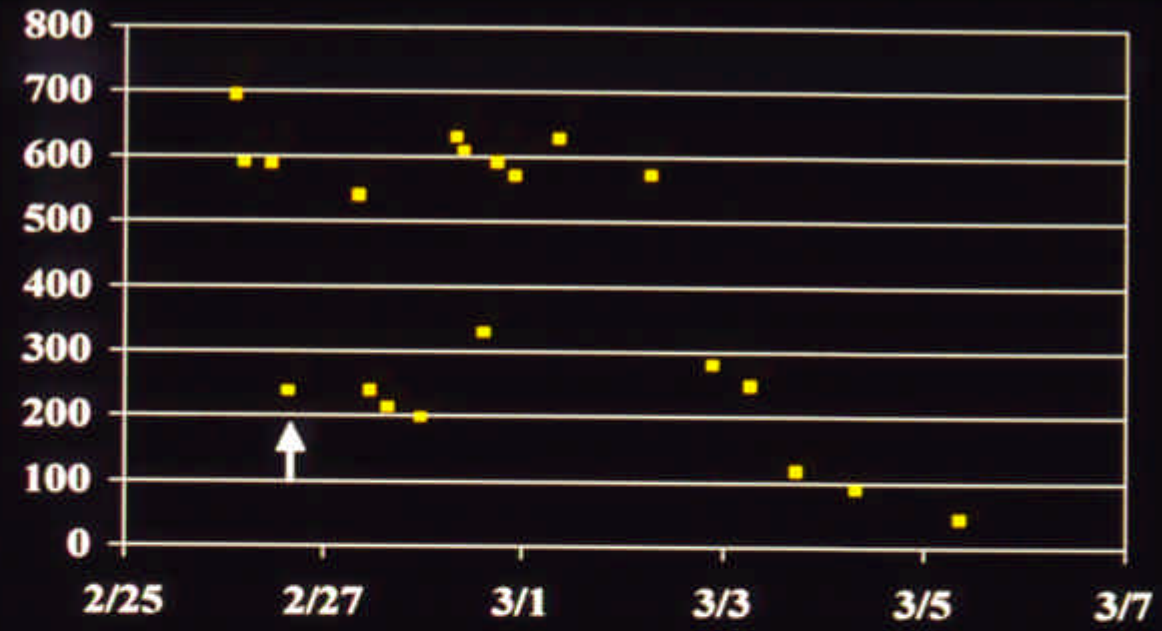
  Other signs

  - Oliguric - 30 mls of urine per hour (<0.5 ml/kg)
  - Weight gain of 12 lb.
  - No edema

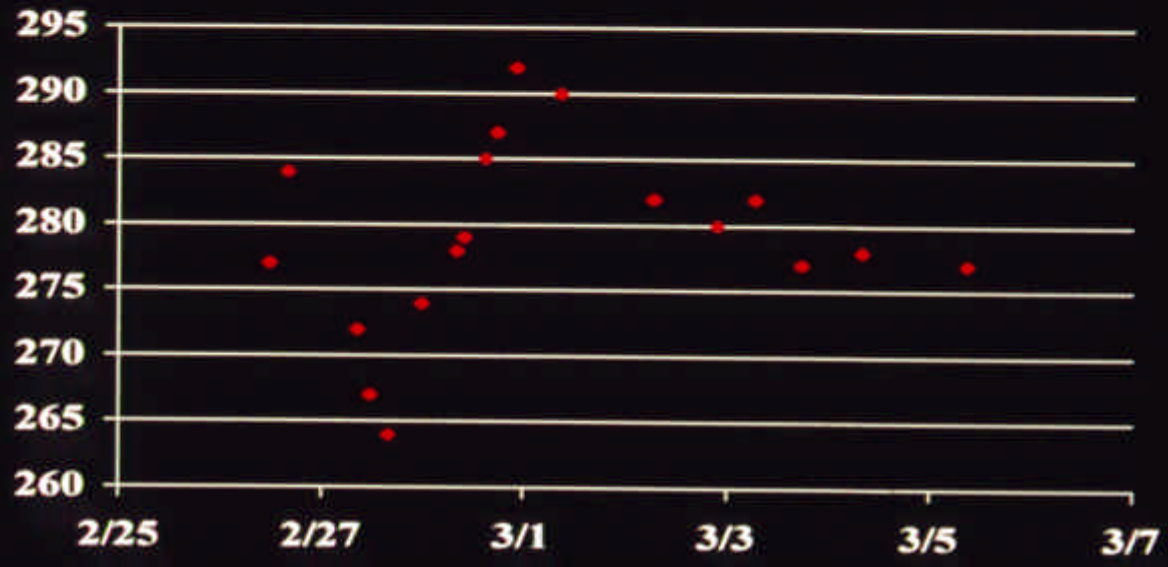
Vinnie

- Key physical Exam Findings
  - Weight gain
  - Decreased urine production
  - No edema
  - Course of neurologic signs
- Key Laboratory Findings
  - Plasma osmolarity 276
  - Urine osmolarity 585
  - Creatinine was 1.13 mg/dl

Urine osmolarity



Plasma osmolarity



Vinnie

- Syndrome of Inappropriate ADH Secretion (SIADH)
- Fluid retention
- Cerebral cellular edema
- Secondary to HIE
- Generally transient

SIADH Therapy

- Goal - Reduction of total body water
- Fluid restriction is the key
  - Intolerable on the long-term
  - Use milk replacer instead of mare's milk
  - Concentrated milk replacer
- Use of furosemide
  - Will increase sodium loss as well as water loss
  - COULD exacerbate problem
- Use of hypertonic saline
  - With acute seizures use small volume
  - Will increase Na 3 to 4 mEq/l with 4-6 ml of the 3%
  - Routine use – exacerbates water and Na overload
- Antagonize ADH
  - Demeclocycline

Vinnie
Clinical Course

- Day 4 early am

  Progressive

  - Couldn't stand, Frantic circles, looses balance

  Treated with furosemide, phenobarbital

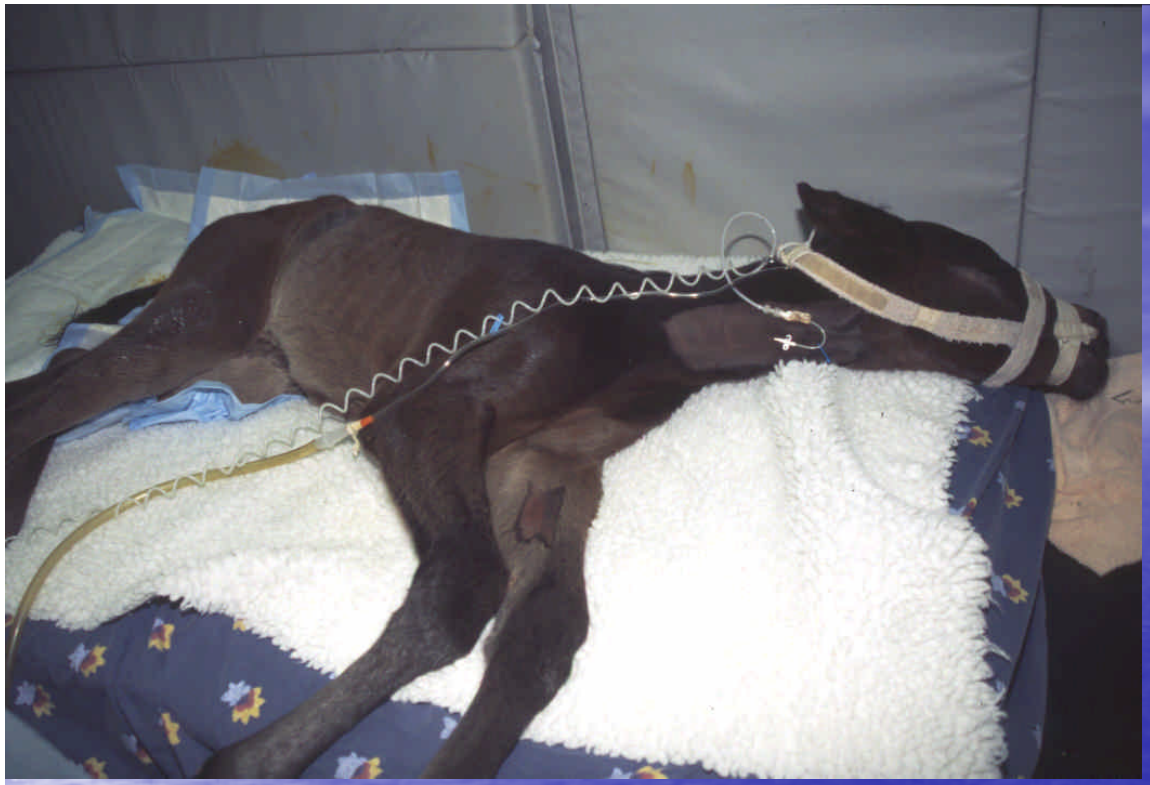
- Day 4

  Began double strength milk replacer

  Behavior improved - lab data low point

- Day 5 & 6

  Dramatic improvement of signs



Speedy

- 8 hr old
- 1 wk post-term

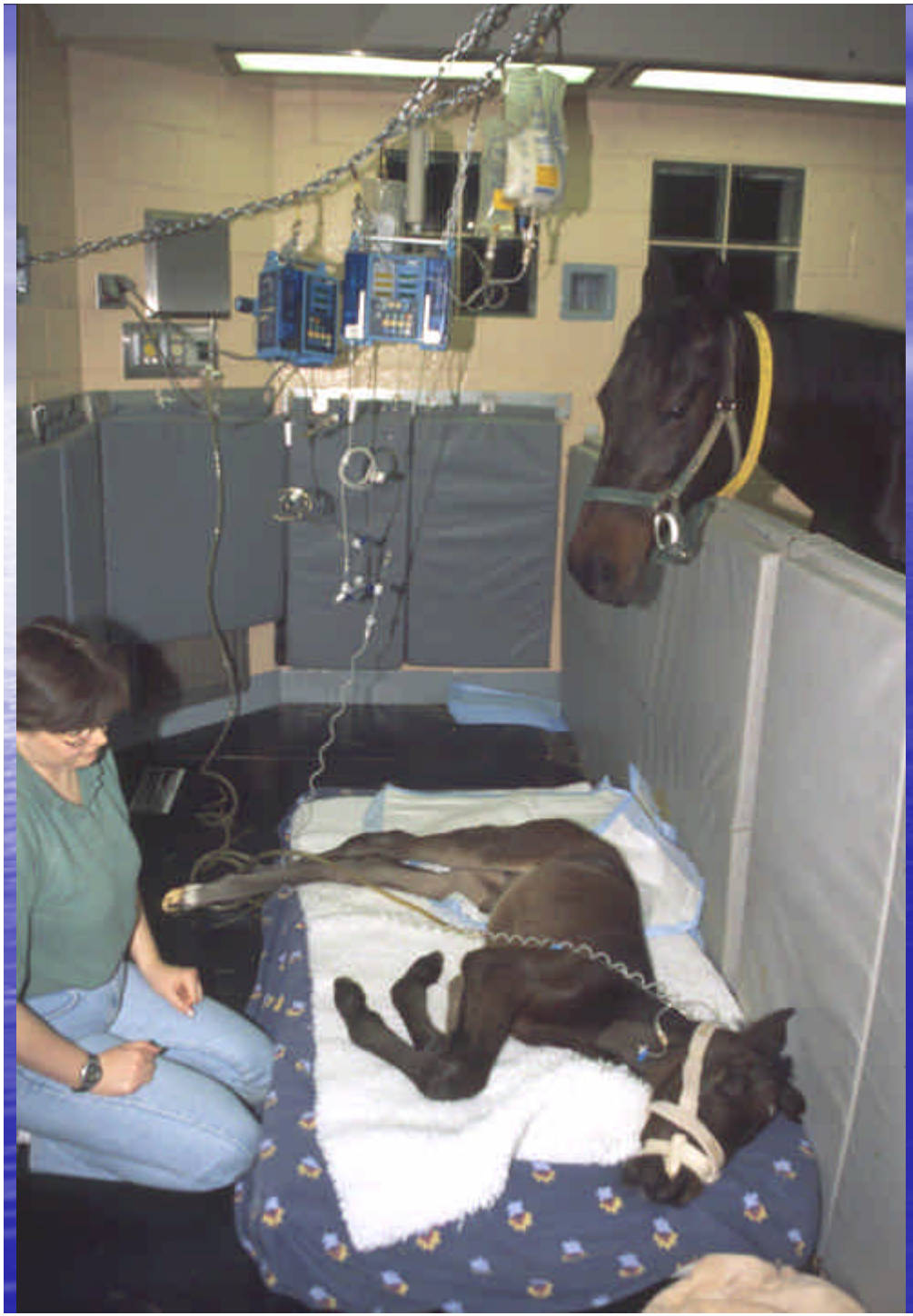
- Problems
  - HIE
    - Apneustic breathing, central hypercapnea
    - Weak, hypertonus, hyperkenetic, hyperresponsive
  - Metabolic maladaptation
  - Neonatal nephropathy
  - Sepsis
  - Neonatal gastroenteropathy

Speedy

- Respiratory acidosis
  pH 7.167, P_{co2} 83
- Hypochloremia (Cl 75 mEq/l)
- Cr (29.32 mg/dl)
- PO4 (24.37 mg/dl)
- Lactate (5.6 mmol/l)
- Ca^{++} (2.33 mg/dl)
  Total Ca 3.46 mg/dl
- Mg^{++} (0.5 mg/dl)

Speedy

- Hypocalcemia
  - Refractory to intravenous Ca therapy
    - 36 hrs of IV Ca therapy
    - No relationship
      - between blood levels and supplement (67-12.5 mg/kg/hr)
  - Responded to Mg therapy
    - Within 5 hrs Ca began to increase
    - PTH effect from ↓Mg

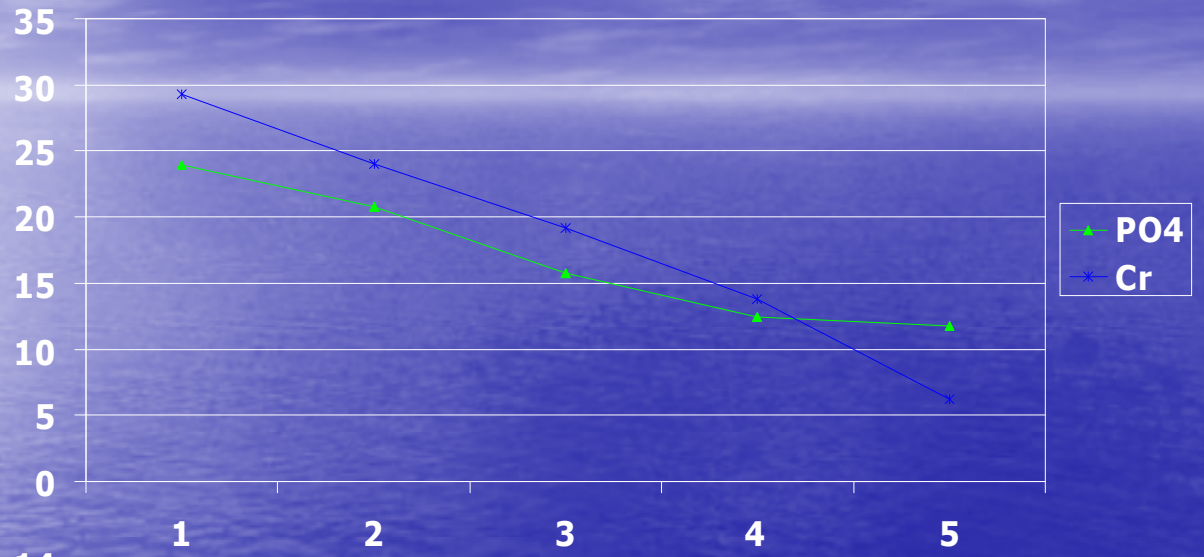


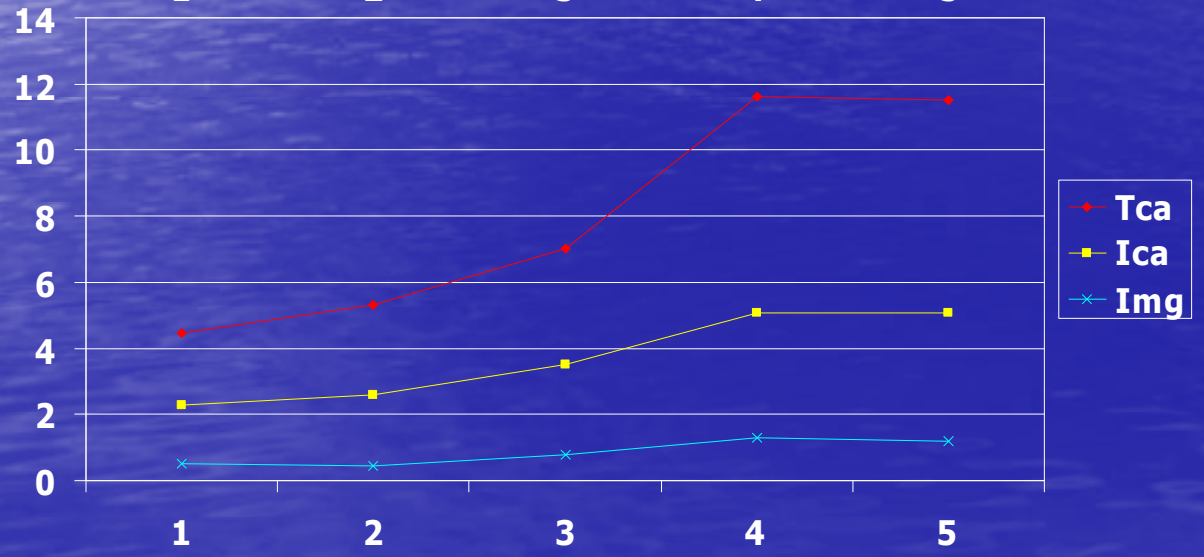
Speedy

- SIDa = 58.7
- SIDe = 78.7
- SIG = +19.9

- Osm_{calc} = 292.7
- $Osm_{measured}$ = 357
- Osm_{Gap} = -64.2

Speedy

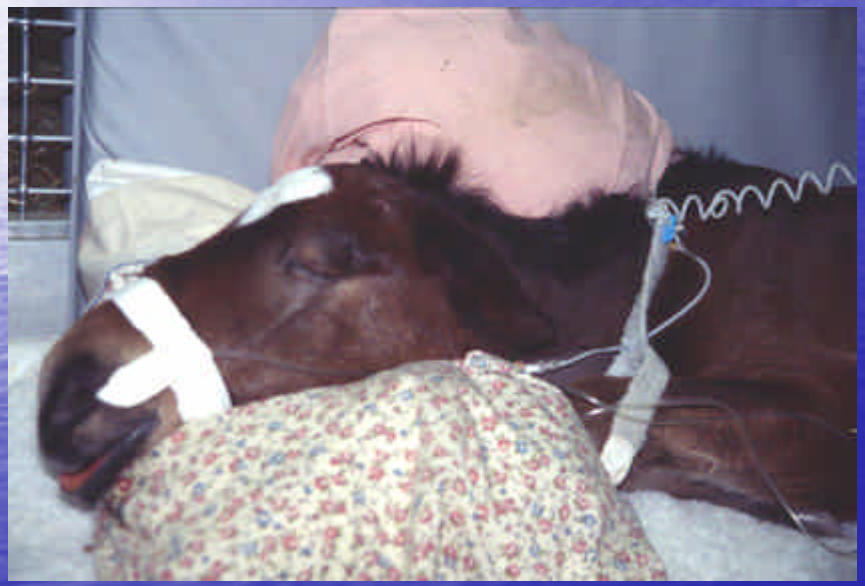




Hyperkalemia
Two Mur

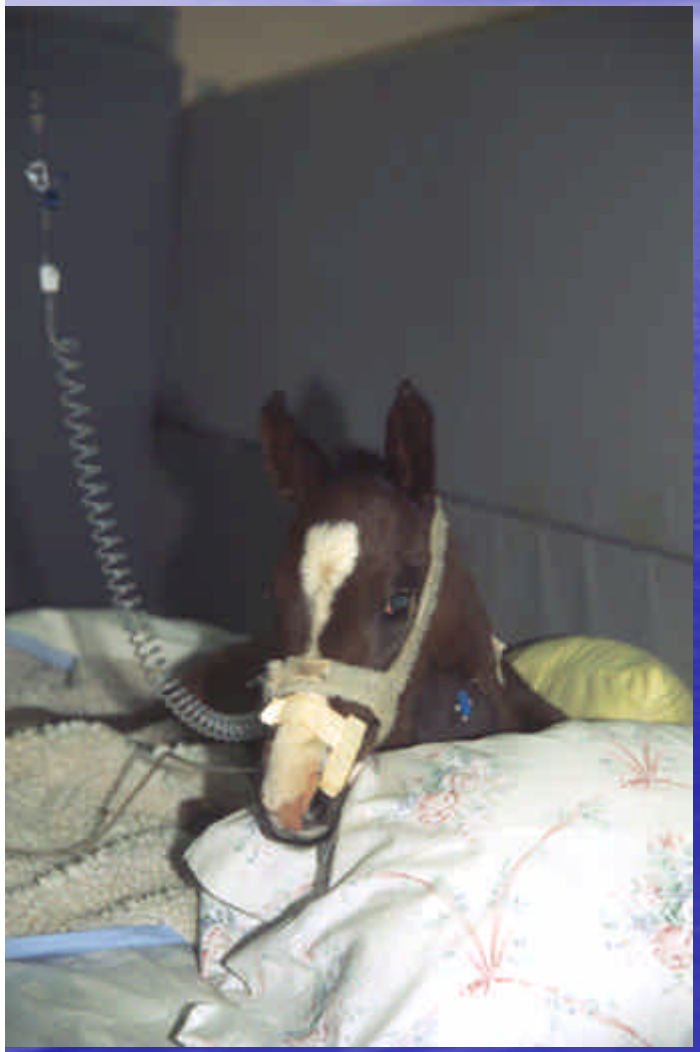
- Gestation
  - Mare had chronic wasting
  - Gestation 378 days
- Mare agalactic
  - Not realized until foal 16 hrs old
- Problems
  - Neonatal encephalopathy
  - SIRS/Sepsis
  - Dysphagia
- Presenting K = 6.78
  - Na = 147
- Osmolarity
  - Osm_{calc} = 308
  - Osm = 323
  - Osm_{Gap} = 14.8

Yankee



- Hx
  - PPS
  - Birth resuscitation by farm manager
  - Weak and legs cold since birth
  - Arrived 14 hrs old
- Problems
  - Neonatal encephalopathy
  - Neonatal gastroenteropathy
  - SIRS - intrauterine
- Presenting K = 6.44, Na = 135
  - Osm_{calc} = 290.5
  - Osm = 314
  - Osm_{Gap} = 23.5

Hugsie

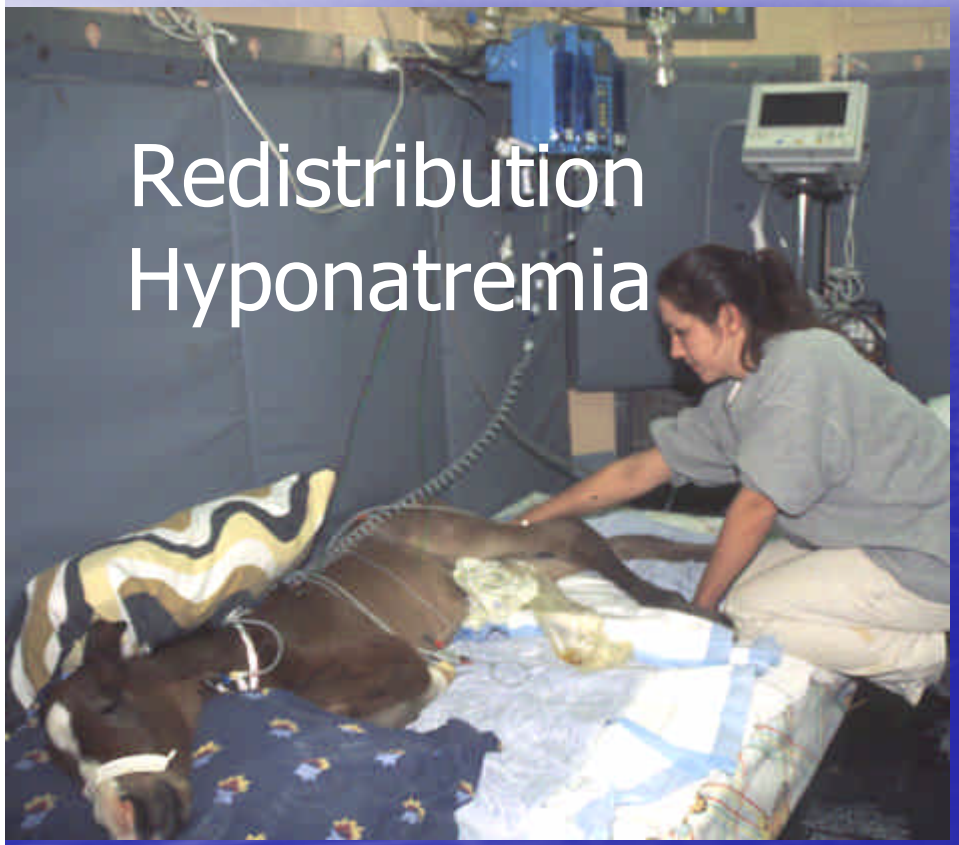


- History
  - Term foal
  - 10 minute stage II
  - Placenta 25 lbs (foal 122 lb)
  - Accompanied sick mare 3 hrs old
- Problems
  - Neonatal encephalopathy
    - Somnolence, hypertonus, seizures
  - Sirs
  - Neonatal gastroenteropathy

Hugsie

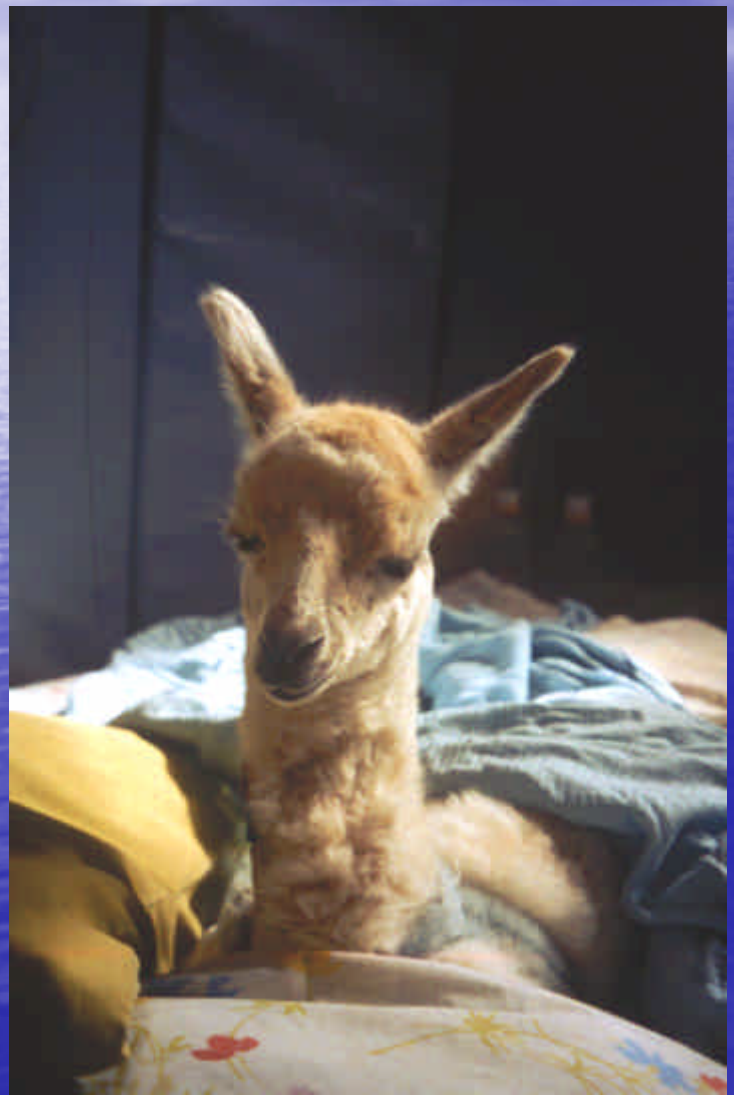
- Progression of signs
  - Edema – Na overload?
    - Fluid overload – ↑ wt 5.9 kg/48 hr
  - Neonatal encephalopathy
    - Progressed to a comatose state
  - Neonatal nephropathy
    - Presenting Cr = 13.6 mg/dl
    - Decreased to 1.12
    - Increased to 3.66
    - F_{xna} increased 0.43% → 6.4%
  - ↑ CPK > 35,000

Hugsie



- Admission
  - Na = 130 mEq/l
  - Cl = 88 mEq/l
  - Osm_c = 274.4 mOsm/l
  - Osm_m = 285 mOsm/l
  - Osm_{gap} = 10.6
- With deterioration
  - Na = 112 mEq/l
  - Cl = 75 mEq/l
  - Osm_c = 242.5 mOsm/l
  - Osm_m = 275mOsm/l
  - Osm_{gap} = 32.4

Hypernatremia
1 week old Cria



- 7 day old cria
  - Mother sick
  - Very hot ambient temperatures
- Clinical signs
  - Weak, depressed, dehydration
- Lab findings
  - Na = 183
  - K = 5.6
  - Cl = 141
  - Osm = 437

Hypernatremia
Origin of the Hypernatremia

- Insensible losses
  - Small body size
    - High surface area to body size ratio
    - High innate metabolic rate
    - High evaporative loss
  - Very hot weather
- Decreased intake
  - Lack of opportunity to nurse
    - Sick mother
  - Hembra's milk production depressed
- High Na intake
  - If hembra is drying off – milk Na ↑

Hypernatremia
1 week old Cria

- Mixed Rx

  Na containing fluids

  D5W

  Milk replacer

  Nursing

    - Clinical signs improved

Hypernatremia
1 week old Cria

- After 21 hrs Rx

  Clinical signs
  - Disorientation, seizures
  - 1 hr later irregular respiratory efforts

  Na = 166 mEq/l (183)
  - 0.81 meq/hr
  - Osm = 397 mosm/l (437)

  K = 4.44 mEq/l (5.6)

  Cl = 134 mEq/l (141)

Electrolyte Abnormalities in Neonates

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Critically ill neonates frequently have electrolyte abnormalities. Usually these are limited to mild disturbances serving as epiphenomena reflecting organ dysfunction (gastrointestinal, renal or endocrine), iatrogenic fluid therapy or feeding mishaps or disorderly transition from fetal to neonatal physiology. Occasionally the disturbances can be severe enough to be life-threatening. The most frequently encountered abnormalities involved sodium, chloride, potassium and calcium.

Sodium/Water Balance

An understanding of the unique sodium handling during the transition from fetal physiology through the neonatal period to adult renal function is important when trying to understand and modify sodium and water balance in the neonate. Neonates require much of the available dietary sodium for bone growth and increase in body mass with the accompanied increase in interstitial space. Although the late term fetus generally has a high fractional excretion of sodium, either before birth (fetal foal) or soon after birth (most other species) the fractional excretion of sodium drops dramatically adapting to a sodium conserving mode. This is appropriate since the neonate's usual diet, milk, is sodium poor. The sodium conservation mode will continue even when the neonate is exposed to a sodium load as may occur while receiving sodium containing intravenous fluids. In such situations, sodium overloading, and expansion of the extracellular fluid space, is a common sequela. Sodium fractional excretion will remain low unless confounding influences such as a glucose diuresis, fluid diuresis from large volume administration of sodium containing fluids, diuretic induced diuresis or renal tubular disease is present. Further complicating the sodium/fluid balance is the neonates difficulty in dealing with volume loading which may occur with fluid therapy. The neonate's inability to rapidly excrete a volume load is both a consequence of fluid shifts between the intravascular and interstitial space and the neonatal kidney's inability excrete the excess volume.

Hyponatremia

When investigating hyponatremia it is convenient to classify the causes as being spurious, dilutional, depletional or secondary to redistribution.

1. *Spurious Hyponatremia*: This form occurs when a low level of plasma sodium is reported from the laboratory despite a normal plasma level present in the patient. This may be from the presence of substances such as lipids or mistakes in sampling such as may occur when a venipuncture site distal to a hypotonic drip is used for sampling or the sample is taken from a catheter used for infusion of a hypotonic solution without sufficient dead space clearing.

2. *Dilutional Hyponatremia*: This form is the most common to occur in neonates and usually results from a lack of balance of fluid intake and urine output as occurs in any loss of integrity of the urinary system (ruptured bladder, fenestrated ureters, etc.), renal failure,

failed or delayed renal transition from fetal to neonatal physiology or water overload as may occur with management mistakes or syndrome of inappropriate antidiuresis (SIA).

3. *Depletional Hyponatremia:* This form commonly occurs when diarrhea results in excessive sodium loss, when sodium wasting occurs in the urine (especially when the neonate is on a milk diet with limited sodium intake), the use of diuretics or endocrine disturbances.

4. *Redistribution Hyponatremia*: In this form, the low sodium occurs secondary to the presence of other osmotically active particles in the plasma drawing fluid out of the intracellular space (redistribution) resulting in an appropriately decreased sodium concentration. This may occur secondary to hyperglycemia, iatrogenic addition of osmoles (e.g. mannitol) or secondary to sick cell syndrome.

Syndrome of Inappropriate Antidiuresis (SIAD)

SIAD, sometimes referred to as SIADH (Syndrome of Inappropriate Antidiuretic Hormone Secretion), results in hyponatremia secondary to inappropriate reabsorption of water from the urine. The diagnosis of SIAD can be made when inappropriately high urine osmolarity occurs in the presence of hyposmolar hyponatremia with normal renal function, normal adrenal function and euvolemia. There may be excessive renal sodium excretion but this is often absent in the neonate because of low sodium intake. Clinically, the syndrome is marked by a sudden decrease in urine output, high urine specific gravity, significant weight gains (10-15% of body weight overnight) without edema and a dropping plasma sodium level. SIAD may be secondary to true inappropriate vasopressin release. The release may be erratic and unpredictable, may be accompanied by a reset of the osmostat (the threshold for release is lowered), vasopressin release may be normal at higher osmolarity but is not fully suppressed at lower osmolarity or vasopressin release may be normal but the receptors are either hypersensitive or continue to respond after vasopressin levels drop (hypovasopressinemic antidiuresis). There are situations where high urine osmolarity occurs in the presence of hyposmolar hyponatremia which mimic inappropriate vasopressin release of which in reality are not. With hypovolemia, appropriate vasopressin release, in defense of volemia, may result in concentrated urine and hyponatremia. Use of diuretics, abnormal adrenal function or abnormal renal function may also result in mimicking clinical scenarios.

Sick Cell Syndrome

Hyponatremia is common in critically ill patients because of loss of cell wall integrity allowing solutes which are normally constrained inside cells to pass into the extracellular space, drawing fluid with them resulting in a dilution of extracellular sodium levels. Redistribution hyponatremia is reflected by the presence of an “Osmolar Gap.” The Osmolar Gap is the difference between calculated and measured osmolarity and reflects the presence of unmeasured osmolites. An Osmolar Gap > 10 mOsm has been associated with multiorgan failure and higher fatality rate in intensive care patients. Although the solutes in question have been thought to be organic phosphate, pyruvate, lactate or amino acids, recent studies have failed to identify any of these as major components.

Hypernatremia

Hypernatremia is less commonly found in the critical neonate. The causes of hypernatremia include spurious, excessive free water loss and iatrogenic. Spurious hypernatremia is usually secondary to sampling errors secondary to withdrawing blood samples from the intravenous catheter without taking a large enough presample resulting in sample contamination with saline. Increased free water loss may be secondary to increased insensible loss in situations where the neonate has an increased respiratory rate in the face of low humidity and a high body temperature or where external warming through radiant heat or hot air heat results in increased evaporative loss. Rarely, maternal milk may have a high sodium content resulting in excessive sodium intake relative to free water. More commonly however, iatrogenic mishaps result in excessive sodium intake relative to free water such as the use of improperly mixed electrolyte solutions, improperly mixed milk replacers (all powdered milk replacers are sodium rich), the use of hypernatremic intravenous fluids solutions (e.g. 5% sodium bicarbonate) or the use of saline in oxygen humidifiers.

Hypochloremia/Hyperchloremia: See section on **"**Metabolic acid/base abnormalities**."**

Hypokalemia

There are in number of reasons why hypokalemia is a common finding in neonates. Potassium is the major intracellular ion. Anabolic increase in cell mass (growth) must be supported by available potassium. Stress/sepsis will also lead to hypokalemia. In the resting state, the muscles are using only about 10% of the available Na+: K+ ATPase activity. It is stimulated acutely by insulin, epinephrine, increased intracellular sodium concentrations and contractile activity. Epinephrine release stimulated by stress/sepsis will stimulate Na+:K+ ATPase activity resulting in significant intracellular shifts of potassium resulting in hypokalemia. The increase ATPase demand will result in increased glucose transport into the cell resulting in increased glucose utilization/requirement and further transport of potassium intracellular. High levels of potassium in milk will support growth requirements, but those foals suffering from stress/sepsis often are the same foals who will not tolerate oral feeding. Any foal requiring parenteral nutrition or prolonged intravenous glucose administration and limited milk feeding will require significant potassium supplementation. Glucocorticoid administration can result in mineralocoritcoid receptor stimulation and significant urine loss of potassium.

Hyperkalemia

Although most clinicians think of a ruptured bladder when they find significant hyperkalemia in the neonatal foal, a second, more common differential is sick cell syndrome. Hyperkalemia will only occur with loss of integrity of the lower urinary tract when the foal is on a milk diet high in potassium. If the foal is receiving parenteral nutrition, hyperkalemia will only occur with overzealous parenteral potassium administration. Foals who have suffered a global cell insult, such as significant perinatal hypoxic ischemic asphyxial insults, may have significant hyperkalemia (as

high as 6-8 mEq/l). Another cause of hyperkalemia can be iatrogenic in the face of renal insufficiency. Mild hyperkalemia can occur secondary to protein catabolism.

Hypocalcemia

Neonates frequently have low plasma ionized calcium levels secondary to the transition from fetal physiology to neonatal physiology. Near term the fetus receives high levels of calcium through active placental transport. At birth, the neonate's homeostatic mechanisms must begin to regulate blood ionized calcium levels. At birth, the parathyroid hormone (PTH) level is low and doesn't increase very quickly. It is slow to respond. PTH requires magnesium and vitamin D, both of which may be initially deficient. At birth, high levels of calcitonin are usually present and asphyxia or prematurity may further increase calcitonin levels. Usually ionized calcium levels decrease during the first hours after birth. Without confounding factors they will stabilize and slowly rise. Neonates who have intrauterine catabolism or are catabolic during the early neonatal period often develop the significant alkalosis which can result in persistently low calcium levels. In general, the neonate is well adapted to these low calcium levels and treatment is not indicated. Extremely low ionized calcium levels at birth suggest significant intrauterine distress.

Hypercalcemia

Because of active placental transport of calcium, ionized calcium is usually quite high at birth (as high as 6-7 mg/dl). These levels are transient (decreasing within hours) unless significant ongoing metabolic acidosis occurs. Foals born with unusually high ionized calcium levels (10-20 mg/dl) may have suffered significant intrauterine distress.

Hypomagnesemia

Magnesium is actively transported across the placenta, but unlike calcium, it's transport can be adversely affected by placental insufficiency and low maternal blood levels. So a neonate may be born with significant hypomagnesemia. Proximately 50% of total body magnesium is and soft tissues in the plasma so low birth magnesium levels reflect total body deficiency and not abnormal homeostasis as is true with calcium. Hypomagnesemia can be accompanied by hypocalcemia and any neonate who is persistently hypocalcemia should be investigated for hypomagnesemia. PTH requires normal magnesium levels to function in bone/serum calcium homeostasis. In such cases, treating the hypocalcemia patient with calcium may exacerbate the problems since calcium will compete with magnesium for transport. Treating with magnesium may readily remedy hypocalcemia. Besides fetal growth retardation, hypomagnesemia is associated with high phosphate levels, diarrhea and excessive renal loss. Also, occasionally extremely hypokalemic patients require magnesium therapy before their potassium will increase.

Hypermagnesemia

Hypermagnesemia is an unusual condition in the neonate except for iatrogenic errors. $MgSO_4$ infusions have become popular in treating hypoxic ischemic encephalopathy, and overzealous treatment may result in high magnesium levels.